Global levels of histone modifications predict prognosis in different cancers.

Journal: Am J Pathol

Publication Year: 2009

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PubMed link: 19349354

Funding Grants: Cellular epigenetic diversity as a blueprint for defining the identity and functional potential of human embryonic stem cells

Public Summary:

Scientific Abstract:
Cancer cells exhibit alterations in histone modification patterns at individual genes and globally at the level of single nuclei in individual cells. We demonstrated previously that lower global/cellular levels of histone H3 lysine 4 dimethylation (H3K4me2) and H3K18 acetylation (ac) predict a higher risk of prostate cancer recurrence. Here we show that the cellular levels of both H3K4me2 and H3K18ac also predict clinical outcome in both lung and kidney cancer patients, with lower levels predicting significantly poorer survival probabilities in both cancer groups. We also show that lower cellular levels of H3K9me2, a modification associated with both gene activity and repression, is also prognostic of poorer outcome for individuals with either prostate or kidney cancers. The predictive power of these histone modifications was independent of tissue-specific clinicopathological variables, the proliferation marker Ki-67, or a p53 tumor suppressor mutation. Chromatin immunoprecipitation experiments indicated that the lower cellular levels of histone modifications in more aggressive cancer cell lines correlated with lower levels of modifications at DNA repetitive elements but not with gene promoters across the genome. Our results suggest that lower global levels of histone modifications are predictive of a more aggressive cancer phenotype, revealing a surprising commonality in prognostic epigenetic patterns of adenocarcinomas of different tissue origins.